AUSTRALIAN PRODUCT INFORMATION – NIMENRIX® (Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine)

1 NAME OF THE MEDICINE

Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

NIMENRIX powder and solvent for solution for injection in pre-filled syringe.

After reconstitution, 1 dose (0.5 mL) contains:

Meningococcal polysaccharide - Group A*	5 micrograms
Meningococcal polysaccharide - Group C*	5 micrograms
Meningococcal polysaccharide - Group W-135*	5 micrograms
Meningococcal polysaccharide - Group Y*	5 micrograms
*conjugated to tetanus toxoid carrier protein	44 micrograms

For the full list of excipients, see Section 6.1 List of excipients.

No preservative or adjuvant is added.

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

The powder or cake is white.

The solvent is clear and colourless.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NIMENRIX is indicated for active immunisation of individuals from 6 weeks of age against invasive meningococcal diseases caused by *Neisseria meningitidis* groups A, C, W-135 and Y.

4.2 Dose and method of administration

NIMENRIX should be used in accordance with available official recommendations.

Dosage

Age Group	Primary Immunisation	Booster
Infants from 6 weeks to less than 6 months of age*[1,2]	Two doses, each of 0.5 ml, with the first dose given from 6 weeks of age, with an interval of 2 months between doses	At 12 months of age
Unvaccinated infants from 6 months to less than 12 months of age**	One dose of 0.5 ml given from 6 months of age	At 12 months of age with a minimum interval of at least 2 months after the primary dose
Children from 12 months of age, adolescents and adults**	One dose of 0.5 ml	Not routinely administered

* See Section 5.1 Pharmacodynamic properties for further information.
**In some situations, consideration may be given to administering an additional primary dose or a booster dose of NIMENRIX (see Section 4.4 Special warnings and precautions for use and Section 5.1 Pharmacodynamic properties for further information).
For further information regarding NIMENRIX Immunisation schedule, please refer to the Australian Immunisation Handbook.

NIMENRIX may be given as a booster dose to individuals who have previously received primary vaccination with NIMENRIX or other conjugated or plain polysaccharide meningococcal vaccines (see Sections 4.4 Special warnings and precautions for use and 5.1 Pharmacodynamic properties).

Method of administration

NIMENRIX is for single use in one patient only.

NIMENRIX is for intramuscular injection only.

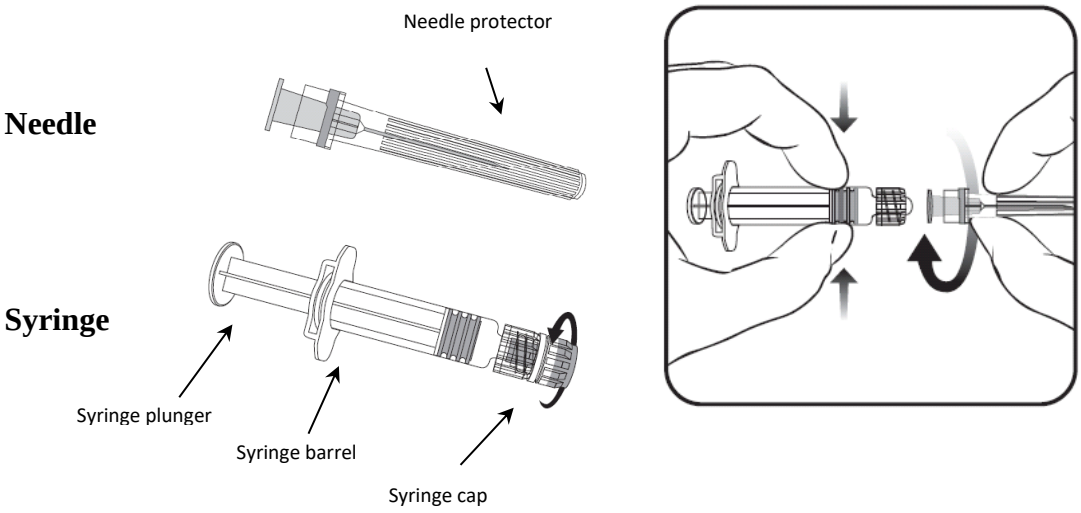
In infants, the recommended injection site is the anterolateral aspect of the thigh. In individuals from 1 year of age, the recommended injection site is the anterolateral aspect of the thigh or deltoid muscle (see Sections 4.4 Special warnings and precautions for use and 4.5 Interactions with other medicines).

Use and handling

Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe

NIMENRIX must be reconstituted by adding the entire contents of the pre-filled syringe of solvent to the vial containing the powder.

To attach the needle to the syringe, refer to the picture below.



1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach a screw-thread needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture). A needle without a screw-thread may also be used. In this case, the needle should be attached without screwing.
3. Remove the needle protector, which on occasion can be a little stiff.
4. Add the solvent to the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.

The reconstituted vaccine is a clear colourless solution.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

After reconstitution, the vaccine should be used promptly. Although delay is not recommended, stability has been demonstrated for 8 hours at 30°C after reconstitution. If not used within 8 hours, do not administer the vaccine.

A new needle should be used to administer the vaccine.

Any unused product or waste material should be disposed of in accordance with local requirements.

4.3 Contraindications

NIMENRIX should not be administered to subjects with hypersensitivity to the active substances or to any of the excipients contained in the vaccine.

4.4 Special warnings and precautions for use

NIMENRIX should under no circumstances be administered intravascularly, intradermally or subcutaneously.

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable effects) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Intercurrent illness

As with other vaccines, vaccination with NIMENRIX should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Syncope

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Thrombocytopenia and coagulation disorders

As with other vaccines administered intramuscularly, NIMENRIX should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

Immunodeficiency

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited.

Persons with certain complement deficiencies and persons receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis* groups A, C, W-135 and Y even if they develop antibodies following vaccination with NIMENRIX.

Special populations

Limited data are available on the safety and immunogenicity in individuals with increased susceptibility to meningococcal infection due to anatomic or functional asplenia (such as sickle cell disease) (see Sections 4.8 Adverse effects and 5.1 Pharmacodynamic properties).

Protection against meningococcal disease

NIMENRIX will only confer protection against *Neisseria meningitidis* groups A, C, W-135 and Y. The vaccine will not protect against other *Neisseria meningitidis* groups.

As with any vaccine, a protective immune response may not be elicited in all vaccines.

Immune response in infants aged 6 months to less than 12 months

A single-dose administered at 6 months was associated with lower human complement serum bactericidal assay (hSBA) titres to groups W-135 and Y compared with three doses administered at 2, 4, and 6 months (see Section 5.1 Pharmacodynamic properties). The clinical relevance of this finding is unknown. If an infant aged 6 months to less than 12 months is expected to be at immediate risk of invasive meningococcal disease due to exposure to groups W-135 and Y, consideration may be given to administering a second primary dose of NIMENRIX after an interval of 2 months.

Immune responses in toddlers aged 12-14 months

At 1 month post vaccination, toddlers aged 12-14 months had similar rabbit complement serum bactericidal assay (rSBA) titres to groups A, C, W-135 and Y following one dose of NIMENRIX or two doses of NIMENRIX given two months apart. At 1 year post vaccination, the rSBA titres for groups A, C, W-135 and Y were similar in both the one and the two dose groups (see Section 5.1 Pharmacodynamic properties).

Measured with a serum bactericidal assay using human complement (hSBA), 1 month post vaccination, responses to groups W-135 and Y were lower after a single dose than after 2 doses given 2 months apart, while responses to groups A and C were similar in the two groups (see Section 5.1 Pharmacodynamic properties). The clinical relevance of these findings is unknown. If a toddler is expected to be at immediate risk of invasive meningococcal disease due to the exposure to groups W-135 and/or Y, consideration may be given to administering a second dose of NIMENRIX after an interval of 2 months.

At 1 year post vaccination, the hSBA responses for groups A, C, W-135 and Y were similar in both the one and the two dose groups (see Section 5.1 Pharmacodynamic properties). Regarding waning of antibody against group A or group C after a first dose of NIMENRIX in children aged 12-23 months, see under Persistence of serum bactericidal antibody titres.

Persistence of serum bactericidal antibody titres

Persistence of antibodies has been evaluated up to 10 years after vaccination. The persistence studies with NIMENRIX have shown a waning of serum bactericidal antibody titres against group A when using hSBA (see Section 5.1 Clinical Trials). The clinical relevance of this observation is unknown. However, if an individual is expected to be at particular risk of exposure to group A and received a dose of NIMENRIX more than approximately 1 year previously, consideration may be given to administering a booster dose.

Similar to the monovalent Men C comparator, a decline in antibody titres over time has been observed for all four serogroups. The clinical relevance of this observation is unknown. A booster dose might be considered in individuals vaccinated at toddler age remaining at high

risk of exposure to meningococcal disease caused by groups A, C, W-135 and Y (see Section 5.1 Pharmacodynamic properties).

Although NIMENRIX contains tetanus toxoid, this vaccine does not substitute for tetanus immunisation.

Use in the elderly

No data available.

Paediatric Use

See Sections 4.1 Therapeutic indications; 4.2 Dose and method of administration; 4.4 Special warnings and precautions for use (see under Protection against meningococcal disease); 4.5 Interactions with other medicines and other forms of interactions; 4.8 Adverse effects and 5.1 Pharmacodynamic properties.

Effects on laboratory tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

In infants, NIMENRIX can be given concomitantly with combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliovirus and Haemophilus influenzae type b vaccines (DTaP/IPV/Hib/HepB), as well as 10-valent pneumococcal conjugate vaccine.

From age 1 and above, NIMENRIX can be given concomitantly with any of the following vaccines: hepatitis A (HAV) and hepatitis B (HBV) vaccines, measles-mumps-rubella (MMR) vaccine, measles-mumps-rubella-varicella (MMRV) vaccine, 10-valent pneumococcal conjugate vaccine or unadjuvanted seasonal influenza vaccine.

NIMENRIX can also be given concomitantly with combined diphtheria-tetanus-acellular pertussis (DTaP) vaccines, including combination DTaP vaccines with hepatitis B, inactivated polio (IPV) or Haemophilus influenzae type b (Hib), such as DTaP/IPV/Hib/HepB vaccine and 13-valent pneumococcal conjugate vaccine in the second year of life.

In individuals aged 9 to 25 years, NIMENRIX can be given concomitantly with human papillomavirus bivalent [Type 16 and 18] vaccine, recombinant (HPV2).

Safety and immunogenicity of NIMENRIX was evaluated when sequentially administered or co-administered with a DTaP/IPV/Hib/HepB vaccine in the second year of life. The administration of NIMENRIX 1 month after the DTaP/IPV/Hib/HepB vaccine resulted in lower MenA, MenC and MenW-135 GMTs as measured with rSBA. The clinical relevance of this observation is unknown, since at least 99.4% of subjects (N=178) had rSBA titres ≥ 8 for each group (A, C, W-135, and Y). Whenever possible, NIMENRIX and a tetanus toxoid (TT) containing vaccine, such as DTaP/IPV/Hib/HepB vaccine, should either be co-

administered or NIMENRIX should be administered at least 1 month before the TT-containing vaccine.

One month after co-administration with a 10-valent pneumococcal conjugate vaccine, lower Geometric Mean antibody Concentrations (GMCs) and opsonophagocytic assay (OPA) antibody GMTs were observed for one pneumococcal serotype (18C conjugated to tetanus toxoid carrier protein). The clinical relevance of this observation is unknown. There was no impact of co-administration on the other nine pneumococcal serotypes.

One month after co-administration with a combined tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine, adsorbed (Tdap) in subjects aged 11 to 25 years, lower GMCs were observed to each pertussis antigen (pertussis toxoid[PT], filamentous haemagglutinin [FHA] and pertactin [PRN]). More than 98% of subjects had anti-PT, FHA or PRN concentrations above the assay cut-off thresholds. The clinical relevance of these observations is unknown. There was no impact of co-administration on immune responses to NIMENRIX or the tetanus or diphtheria antigens included in Tdap.

If NIMENRIX is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

As with other vaccines, it may be expected that in patients receiving immunosuppressive treatment an adequate response may not be elicited.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Animal studies with NIMENRIX do not indicate direct or indirect harmful effects with respect to fertility (see Section 5.3 Preclinical safety data).

Use in pregnancy - Pregnancy Category B2

There is limited experience with use of NIMENRIX in pregnant women.

Animal studies with NIMENRIX do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see Section 5.3 Preclinical safety data).

NIMENRIX should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.

Use in lactation

The safety of NIMENRIX when administered to breastfeeding women has not been evaluated. It is unknown whether NIMENRIX is excreted in human breast milk.

NIMENRIX should only be used during breast-feeding when the possible advantages outweigh the potential risks.

4.7 Effects on ability to drive and use machines

No studies on the effects of NIMENRIX on the ability to drive and use machines have been performed.

4.8 Adverse effects (undesirable effects)

Clinical trial data

The safety of NIMENRIX presented in the table below is based on two clinical study datasets as follows:

- A pooled analysis of data from 9,621 subjects administered a single dose of NIMENRIX. This total included 3,079 toddlers (12 months to 23 months), 909 children between 2 and 5 years of age, 990 children between 6 and 10 years of age, 2,317 adolescents (11 to 17 years) and 2,326 adults (18 to 55 years). In a separate study a single dose of NIMENRIX was administered to 274 individuals aged 56 years and older.
- Data from a study in infants aged 6 to 12 weeks at the time of the first dose (Study MenACWY-TT-083), 1,052 subjects received at least one dose of a primary series of 2 or 3 doses of NIMENRIX and 1,008 received a booster dose at approximately 12 months of age.

Local and general adverse reactions

In all age groups, the local adverse reactions of pain, redness and swelling at the injection site were reported at a very common frequency after vaccination.

In the infant and toddler groups, the general adverse reactions of drowsiness, fever, irritability/fussiness and loss of appetite were reported at a very common frequency after vaccination.

In an additional clinical study of age matched subjects who were either healthy or at increased risk of meningococcal disease due to anatomical or functional asplenia (such as sickle cell disease), the safety profile of NIMENRIX in at-risk children and adolescents was generally similar to that observed in the non-asplenic population (see 5.1 Pharmacodynamic properties).

In a separate infant study, 554 infants were primed with 1 or 3 doses of NIMENRIX and 508 received booster doses in the second year of life. Local and general adverse reactions in this study were similar in frequency to the larger infant study.

In the 12-14 months age group who received 2 doses of NIMENRIX given 2 months apart, the first and second doses were associated with similar local and systemic reactogenicity.

The 2–5 year group reported general adverse reactions at a frequency ranging from common (irritability, loss of appetite and fever) to very common (drowsiness).

In the 6-10, 11-17 and ≥ 18 years age groups, the general adverse reactions were reported at a frequency ranging from common (gastrointestinal symptoms and fever) to very common (headache and fatigue).

In a clinical study of 11 to 25 year old subjects co-administered NIMENRIX and Tdap or given the vaccines separately, the local reactions (injection site pain, redness, and swelling) and general reactions (fatigue and headache) occurred at a similar frequency in both groups and in the subjects in the pooled analysis (very common). The general reactions gastrointestinal events (nausea, vomiting, diarrhoea, abdominal pain) occurred more frequently (very common) and fever occurred less frequently (common) compared to subjects in the pooled analysis, but occurred at a similar frequency in subjects co-administered the vaccines and subjects given the vaccines separately in the study.

In a clinical study of female subjects 9 to 25 years old, the local reactions (pain, redness, and swelling at the NIMENRIX injection site) and general reactions (headache, fever, and fatigue) occurred at a similar frequency in subjects co-administered NIMENRIX, Tdap and HPV2 and in subjects given NIMENRIX alone, as they did in subjects in the pooled analysis (very common). The general reactions gastrointestinal events (nausea, vomiting, diarrhoea, abdominal pain) and myalgia occurred at a similar frequency in the 2 groups but more frequently than in the pooled analysis (very common), as did the general reaction rash (common).

The local and general adverse reaction profile of a booster dose of NIMENRIX given to subjects from 12 months of age after primary vaccination with NIMENRIX or other conjugated or plain polysaccharide meningococcal vaccines, was similar to the local and general adverse reaction profile observed after primary vaccination with NIMENRIX, except gastrointestinal symptoms (including diarrhoea, vomiting, and nausea) which ranged from common to very common among subjects 6 years of age and older (versus common after primary vaccination).

Tabulated list of Adverse reactions

Adverse reactions reported are listed according to the following frequency:

Very common ≥ 1/10
Common ≥ 1/100 to < 1/10
Uncommon ≥ 1/1,000 to < 1/100
Rare ≥ 1/10,000 to < 1/1,000
Very rare < 1/10,000
Not known (cannot be estimated from the available data)

Table 1: Tabulated summary of adverse reactions by system organ class

System Organ Class	Frequency	Adverse reactions
Metabolism and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability
	Uncommon	Insomnia Crying

Nervous system disorders	Very common	Drowsiness Headache
	Uncommon	Hypoaesthesia Dizziness
Gastrointestinal disorders	Common	Diarrhoea Vomiting Nausea*
Skin and subcutaneous tissue disorders	Uncommon	Rash** Urticaria Pruritus
Musculoskeletal and connective tissue disorders	Uncommon	Myalgia Pain in extremity
General disorders and administration site conditions	Very common	Fever Swelling Pain at injection site Redness at injection site Fatigue
	Common	Injection site haematoma*
	Uncommon	Malaise Injection site induration Injection site pruritus Injection site warmth Injection site anaesthesia
	Not known***	Extensive limb swelling at the injection site, frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb

*Nausea and injection site haematoma occurred at a frequency of Uncommon in infants
**Rash occurred at a frequency of Common in infants
The adverse reactions headache, hypoaesthesia, dizziness, pruritus, myalgia, pain in extremity and fatigue were not reported in the infant clinical study.
***ADR identified post-marketing

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://www.tga.gov.au/reporting-problems.

4.9 Overdose

No cases of overdose have been reported.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Anti-capsular meningococcal antibodies protect against meningococcal disease via complement mediated bactericidal activity. NIMENRIX induces the production of bactericidal antibodies against capsular polysaccharides of *Neisseria meningitidis* groups A, C, W-135 and Y when measured by serum bactericidal antibody assays (SBA) using either rSBA or human complement (hSBA). By conjugating capsular polysaccharide to a protein carrier that contains T-cell epitopes, meningococcal conjugate vaccines like NIMENRIX change the nature of the immune response to capsular polysaccharide from T-cell independent to T-cell dependent.

Clinical trials

Immunogenicity in infants

Two clinical studies have been conducted in infants, MenACWY-TT-083 and MenACWY-TT-087. In Study MenACWY-TT-083, the immunogenicity of a 2-dose primary vaccination schedule administered at 2 and 4 months of age was evaluated. Routinely used infant vaccines DTaP/IPV/Hib/HepB and a 10-valent pneumococcal vaccine were co-administered. For group C, rSBA and hSBA titres elicited by NIMENRIX were compared to a 2-dose priming with licensed monovalent meningococcal conjugate group C vaccines, MenC-CRM and MenC-TT vaccines. NIMENRIX elicited rSBA and hSBA titres against the four meningococcal groups. The response against group C was non-inferior to the one elicited by the licensed MenC-CRM and MenC-TT vaccines in terms of the percentage of subjects with rSBA titres ≥8 at 1 month after the second dose.

For subjects initially vaccinated in infancy with NIMENRIX at 2 and 4 months of age and receiving a NIMENRIX booster dose at 12 months of age, the increase in rSBA and hSBA titres 1 month post-booster dose ranged between 15 and 80-fold for all groups (Study MenACWY-TT-083) and more than 99.0% of all infants achieved post-booster titres above 8 for both assays. The observed booster response for group C was similar to that observed in subjects primed and boosted with a monovalent MenC conjugate vaccine (TT or CRM conjugated). Results are shown in Table 2.

Table 2: rSBA and hSBA titres following two doses of NIMENRIX (or MenC-CRM or MenC-TT) given 2 months apart with the first dose administered to infants 6-12 weeks of age and following a booster at 12 months of age (Study MenACWY-TT-083)

Meningococcal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	**NIMENRIX**	Post dose 2	456	97.4% (95.4; 98.6)	203 (182; 227)	202	96.5% (93.0; 98.6)	157 (131; 188)
	NIMENRIX	Booster dose	462	99.6% (98.4; 99.9)	1561 (1412; 1725)	214	99.5% (97.4;100)	1007 (836;1214)
C	**NIMENRIX**	Post dose 2	456	98.7% (97.2; 99.5)	612 (540; 693)	218	98.6% (96.0; 99.7)	1308 (1052; 1627)
		Booster dose	463	99.8% (98.8; 100)	1177 (1059; 1308)	221	99.5% (97.5; 100)	4992 (4086; 6100)
	MenC-CRM vaccine	Post dose 2	455	99.6% (98.4; 99.9)	958 (850; 1079)	202	100% (98.2; 100)	3188 (2646; 3841)
		Booster dose	446	98.4% (96.8; 99.4)	1051 (920; 1201)	216	100% (98.3; 100)	5438.2 (4412; 6702)
	MenC-TT vaccine	Post dose 2	457	100% (99.2; 100)	1188 (1080; 1307)	226	100% (98.4; 100)	2626 (2219; 3109)
		Booster dose	459	100% (99.2; 100)	1960.2 (1776; 2163)	219	100% (98.3; 100)	5542 (4765; 6446)
W-135	**NIMENRIX**	Post dose 2	455	99.1% (97.8; 99.8)	1605 (1383; 1862)	217	100% (98.3; 100)	753 (644; 882)
		Booster dose	462	99.8% (98.8; 100)	2777.2 (2485; 3104)	218	100% (98.3; 100)	5122.7 (4504; 5826)
Y	**NIMENRIX**	Post dose 2	456	98.2% (96.6; 99.2)	483 (419; 558)	214	97.7% (94.6; 99.2)	328 (276; 390)
		Booster dose	462	99.4% (99.1; 99.9)	881.3 (788; 986)	217	100% (98.3; 100)	2954 (2498; 3493)

The analysis of immunogenicity was conducted on the primary according-to-protocol (ATP) cohort

*rSBA analysis performed at Public Health England (PHE) laboratories in UK

**hSBA analysis performed at GSK laboratories

In MenACWY-TT-087, infants received either a single primary dose at 6 months followed by a booster dose at 15-18 months or three primary doses at 2, 4, and 6 months followed by a booster dose at 15-18 months. All subjects also received DTPa-IPV/Hib and 10-valent pneumococcal conjugate vaccines at all time points. A single primary dose administered at 6 months of age elicited robust rSBA responses to groups A, C, W-135 and Y, as measured

by the percentage of subjects with rSBA titres ≥8, that were comparable to responses after the last dose of a three-dose primary series. A booster dose produced robust responses, comparable between the two dosing groups, against all four meningococcal groups (Table 3).

Table 3: Bactericidal antibody responses (rSBA*) and (hSBA) in infants after one dose at 6 months of age and after a booster dose at 15-18 months of age (Study MenACWY-TT-087)**

Meningo-coccal Group		rSBA*			hSBA**		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Post dose 1[(1)]	163	98.8% (95.6; 99.9)	1332.9 (1035.2; 1716.2)	59	98.3% (90.9; 100)	270.5 (205.9; 355.4)
	Pre Booster	131	81.7% (74.0; 87.9)	125.3 (84.4; 186.1)	71	66.2% (54.0; 77.0)	20.8 (13.5; 32.2)
	Post booster[(1)]	139	99.3% (96.1; 100)	2762.3 (2310.3; 3302.8)	83	100% (95.7; 100)	1415.6 (1140.2; 1757.5)
C	Post dose 1[(1)]	163	99.4% (96.6; 100)	591.6 (482.3; 725.8)	66	100% (94.6;100)	523.1 (381.5; 717.3)
	Pre Booster	131	65.6% (56.9; 73.7)	27.4 (20.6; 36.6)	78	96.2% (89.2; 99.2)	150.8 (108.5; 209.5)
	Post booster[(1)]	139	99.3% (96.1; 100)	2525.2 (2102.1; 3033.3)	92	100% (96.1; 100)	13360.1 (10952.9; 16296.4)
W	Post dose 1[(1)]	163	93.9% (89.0; 97.0)	1255.9 (917.0; 1720.0)	47	87.2% (74.3; 95.2)	136.5 (78.4; 237.6)
	Pre Booster	131	77.9% (69.8; 84.6)	63.3 (45.6; 87.9)	53	100% (93.3; 100)	428.6 (328.4; 559.2)
	Post booster[(1)]	139	100% (97.4; 100)	3144.7 (2636.9; 3750.4)	59	100% (93.9; 100)	9015.6 (7045.2; 11537.1)
Y	Post dose 1[(1)]	163	98.8% (95.6; 99.9)	1469.9 (1186.5; 1821.0)	52	92.3% (81.5; 97.9)	194.8 (117.6; 322.9)
	Pre Booster	131	88.5% (81.8; 93.4)	106.4 (76.4; 148.1)	61	98.4% (91.2; 100)	389.2 (292.3; 518.1)
	Post booster[(1)]	139	100% (97.4; 100)	2748.6 (2301.4; 3282.6)	69	100% (94.8; 100)	5977.6 (4746.8; 7527.6)

The analysis of immunogenicity was conducted on the primary according-to-protocol (ATP) cohort for immunogenicity.

*rSBA testing performed at Public Health England (PHE) laboratories in UK

**hSBA tested at Neomed, Laval, Canada

[(1)] blood sampling performed 1 month post vaccination

Serum bactericidal activity was also measured using hSBA as a secondary endpoint. Although similar responses to groups A and C were observed with both dosing schedules, a

single primary dose in infants at 6 months was associated with lower hSBA responses to groups W-135 and Y as measured by the percentage of subjects with hSBA titres ≥8 [87.2% (95% CI: 74.3, 95.2) and 92.3% (95% CI: 81.5, 97.9), respectively] compared with three primary doses at 2, 4, and 6 months of age [100% (95% CI: 96.6, 100) and 100% (95% CI: 97.1, 100), respectively] (see Section 4.4 Special warnings and precautions for use). After a booster dose, the hSBA titres to all four serogroups were comparable between the two dosing schedules.

Immunogenicity in toddlers aged 12-23 months

In clinical studies MenACWY-TT-039 and MenACWY-TT-040, the immune response to vaccination with one dose of NIMENRIX or a licensed meningococcal C-CRM_{197} conjugate (MenC-CRM) vaccine was evaluated.

NIMENRIX elicited SBA titres against the four meningococcal groups, with group C rSBA titres that were comparable to those elicited by a licensed MenC-CRM vaccine in terms of the percentage of subjects with rSBA titres ≥8. In Study MenACWY-TT-039, hSBA was also measured as a secondary endpoint. Results are shown in Table 4.

Table 4: SBA* titres following a single dose of NIMENRIX (or MenC-CRM) in toddlers aged 12-23 months (Studies MenACWY-TT-039/040)

Meningococcal group	Vaccine Group	Study MenACWY-TT-039[(1)]						Study MenACWY-TT-040[(2)]		
		rSBA*			hSBA*			rSBA*		
		N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	**NIMENRIX**	354	99.7% (98.4; 100)	2205 (2008; 2422)	338	77.2% (72.4; 81.6)	19.0 (16.4; 22.1)	183	98.4% (95.3; 99.7)	3170 (2577; 3899)
C	**NIMENRIX**	354	99.7% (98.4; 100)	478 (437; 522)	341	98.5% (96.6; 99.5)	196 (175; 219)	183	97.3% (93.7; 99.1)	829 (672; 1021)
	MenC-CRM vaccine	121	97.5% (92.9; 99.5)	212 (170; 265)	116	81.9% (73.7; 88.4)	40.3 (29.5; 55.1)	114	98.2% (93.8; 99.8)	691 (521; 918)
W-135	**NIMENRIX**	354	100% (99.0; 100)	2682 (2453; 2932)	336	87.5% (83.5 ; 90.8)	48.9 (41.2; 58.0)	186	98.4% (95.4; 99.7)	4022 (3269; 4949)
Y	**NIMENRIX**	354	100% (99.0; 100)	2729 (2473; 3013)	329	79.3% (74.5; 83.6)	30.9 (25.8; 37.1)	185	97.3% (93.8; 99.1)	3168 (2522; 3979)

The analysis of immunogenicity was conducted on the according-to-protocol (ATP) cohorts

(1) blood sampling performed 42 to 56 days post vaccination

(2) blood sampling performed 30 to 42 days post vaccination

*SBA analyses performed at GSK laboratories

N = number of subjects with available results

GMT = geometric mean antibody titre

In Study Men ACWY-TT-104, NIMENRIX elicited rSBA titres against all four meningococcal groups following one or two doses administered 2 months apart that were similar in terms of the percentage of subjects with rSBA titre ≥8 and GMT. Results are shown in Table 5.

Table 5: rSBA and hSBA titres following one or two doses of NIMENRIX with the first dose administered to toddlers aged 12-14 months (Study MenACWY-TT-104)

Meningo-coccal group	Nimenrix dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	1 dose	1 Month Post dose 1	180	97.8% (94.4; 99.4)	1437 (1118; 1847)	74	95.9% (88.6; 99.2)	118 (86.8; 161)
		1 Year Post dose 1	167	63.5% (55.7; 70.8)	62.7 (42.6; 92.2)	70	35.7% (24.6; 48.1)	6.1 (4.1; 8.9)
	2 doses	1 Month Post dose 1	158	96.8% (92.8; 99.0)	1275 (970; 1675)	66	97.0% (89.5; 99.6)	133 (98.1; 180)
		1 Month Post dose 2	150	98.0% (94.3; 99.6)	1176 (922; 1501)	66	97.0% (89.5; 99.6)	171 (126; 230)
		1 Year Post dose 2	143	70.6% (62.4; 77.9)	76.6 (50.7; 116)	62	35.5% (23.7; 48.7)	6.4 (4.2; 10.0)
C	1 dose	1 Month Post dose 1	179	95.0% (90.7; 97.7)	452 (345.6; 591.9)	78	98.7% (93.1; 100)	152 (105; 220)
		1 Year Post dose 1	167	49.1% (41.3; 56.9)	16.2 (12.4; 21.1)	71	80.3% (69.1; 88.8)	35.2 (22.5; 55.2)
	2 doses	1 Month Post dose 1	157	95.5% (91.0; 98.2)	369 (281; 486)	70	95.7% (88.0; 99.1)	161 (110; 236)
		1 Month Post dose 2	150	98.7% (95.3; 99.8)	639 (522; 783)	69	100% (94.8; 100)	1753 (1278; 2404)
		1 Year Post dose 2	143	55.2% (46.7; 63.6)	21.2 (15.6; 28.9)	63	90.5% (80.4; 96.4)	73.4 (47.5; 113.4)
W-135	1 dose	1 Month Post dose 1	180	95.0% (90.8; 97.7)	2120 (1601; 2808)	72	62.5% (50.3; 73.6)	27.5 (16.1; 46.8)
		1 Year Post dose 1	167	65.3% (57.5; 72.5)	57.2 (39.9; 82.0)	72	95.8% (88.3; 99.1)	209 (150; 291)
W-135	2 doses	1 Month Post dose 1	158	94.9% (90.3; 97.8)	2030 (1511; 2728)	61	68.9% (55.7; 80.1)	26.2 (16.0; 43.0)
		1 Month Post dose 2	150	100% (97.6; 100)	3533 (2914; 4283)	70	97.1% (90.1; 99.7)	757 (550; 1041)
		1 Year Post dose 2	143	77.6% (69.9; 84.2)	123 (82.7; 183)	65	98.5% (91.7; 100.0)	233 (168; 321)
Y	1 dose	1 Month Post dose 1	180	92.8% (88.0; 96.1)	952 (705; 1285)	71	67.6% (55.5; 78.20)	41.2 (23.7; 71.5)
		1 Year Post dose 1	167	73.1% (65.7; 79.6)	76.8 (54.2; 109)	62	91.9% (82.2; 97.3)	144 (97.2; 215)
	2 doses	1 Month Post dose 1	157	93.6% (88.6; 96.9)	933 (692; 1258)	56	64.3% (50.4; 76.6)	31.9 (17.6; 57.9)
		1 Month Post dose 2	150	99.3% (96.3; 100)	1134 (945; 1360.5)	64	95.3% (86.9; 99.0)	513 (339; 775)

Meningo-coccal group	Nimenrix dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		1 Year Post dose 2	143	79.7% (72.2; 86.0)	112 (77.5; 163)	58	87.9% (76.7; 95.0)	144 (88.5; 234)

The analysis of immunogenicity was conducted on the ATP cohort

[(1)] blood sampling performed 21-48 days post vaccination and 44-60 weeks post vaccination

* rSBA analysis performed at PHE laboratories

**hSBA analysis performed at GSK laboratories

In Study MenACWY-TT-104, hSBA titres were measured as a secondary endpoint. In terms of the percentage of subjects with hSBA titres ≥8, at 1 month post vaccination, hSBA titres against groups W-135 and Y were higher after two doses of NIMENRIX than after one dose, while the hSBA titres against groups A and C were similar in the two dose groups. At 1 year post vaccination, the percentage of subjects with hSBA titres ≥8 for all four meningococcal groups were similar in both the one and two dose groups (Table 5).

Immunogenicity in children aged 2-10 years

In two comparative studies of non-inferiority conducted in subjects aged 2-10 years, one dose of NIMENRIX was compared to either the licensed ACWY-PS vaccine (Study MenACWY-TT-038) or a licensed MenC-CRM vaccine (Study MenACWY-TT-081).

In Study MenACWY-TT-038, a single dose of NIMENRIX was demonstrated to be non-inferior to the licensed ACWY-PS vaccine in terms of vaccine response to the four meningococcal groups as shown in Table 6.

Table 6: rSBA* titres following a single dose of NIMENRIX or ACWY-PS in children aged 2-10 years (Study MenACWY-TT-038)

Meningococcal group	NIMENRIX[(1)]			ACWY-PS vaccine[(1)]		
	N	VR (95%CI)	GMT (95%CI)	N	VR (95%CI)	GMT (95%CI)
A	594	89.1% (86.3 91.5)	6343 (5998; 6708)	192	64.6% (57.4; 71.3)	2283 (2023; 2577)
C	691	96.1% (94.4; 97.4)	4813 (4342; 5335)	234	89.7% (85.1; 93.3)	1317 (1043; 1663)
W-135	691	97.4% (95.9; 98.4)	11543 (10873; 12255)	236	82.6% (77.2; 87.2)	2158 (1815; 2565)
Y	723	92.7% (90.5; 94.5)	10825 (10233; 11452)	240	68.8% (62.5; 74.6)	2613 (2237; 3052)

The analysis of immunogenicity was conducted on the ATP cohort

[(1)] Blood sampling performed 1 month post vaccination

VR: vaccine response, defined as the proportion of subjects with:

- rSBA titres ≥ 32 for initially seronegative subjects (i.e., pre-vaccination rSBA titre <8)
- at least a 4-fold increase in rSBA titres from pre- to post-vaccination for initially seropositive subjects (i.e., pre vaccination rSBA titre ≥8)

*rSBA analysis performed at GSK laboratories

N = number of subjects with available results

GMT = geometric mean antibody titre

In Study MenACWY-TT-081, a single dose of NIMENRIX (N=268) was demonstrated to be non-inferior to a licensed MenC-CRM vaccine (N=92) in 2 to 10 year olds in terms of group C vaccine response one month post-vaccination [94.8% (95% CI: 91.4; 97.1) and 95.7% (95% CI: 89.2; 98.8) respectively]. Group C geometric mean titres (GMTs) were lower for the NIMENRIX group [2795 (95% CI: 2393; 3263)] versus the MenC-CRM group [5292 (95% CI: 3815; 7340)].

Immunogenicity in adolescents aged 11-17 years and adults aged ≥ 18

In two clinical studies, one dose of NIMENRIX was compared to one dose of ACWY-PS vaccine administered to adolescents aged 11-17 years (Study MenACWY-TT-036) and in adults aged 18-55 years (Study MenACWY-TT-035).

In both adolescents and adults, NIMENRIX was demonstrated to be immunologically non-inferior to the ACWY-PS vaccine in terms of vaccine response. The rSBA titres to the four meningococcal groups elicited by NIMENRIX were either similar to or higher than those elicited by the ACWY-PS vaccine as shown in Table 7.

Table 7: Bactericidal antibody responses (rSBA* titres) following a single dose of NIMENRIX or ACWY-PS in adolescents aged 11-17 years and adults aged 18 – 55 years inclusive (Studies MenACWY-TT-035/036) one month after vaccination

Meningo-coccal group	Vaccine group	Study MenACWY-TT-036 (11-17 years)[(1)]			Study MenACWY-TT-035 (18-55 years)[(1)]		
		N	VR (95% CI)	GMT (95% CI)	N	VR (95% CI)	GMT (95% CI)
A	NIMENRIX	553	85.4% (82.1; 88.2)	5928 (5557; 6324)	743	80.1% (77.0; 82.9)	3625 (3372; 3897)
	ACWY-PS vaccine	191	77.5% (70.9; 83.2)	2947 (2612; 3326)	252	69.8% (63.8; 75.4)	2127 (1909; 2370)
C	NIMENRIX	642	97.4% (95.8; 98.5)	13110 (11939; 14395)	849	91.5% (89.4; 93.3)	8866 (8011; 9812)
	ACWY-PS vaccine	211	96.7% (93.3; 98.7)	8222 (6807; 9930)	288	92.0% (88.3; 94.9)	7371 (6297; 8628)
W-135	NIMENRIX	639	96.4% (94.6; 97.7)	8247 (7639; 8903)	860	90.2% (88.1; 92.1)	5136 (4699; 5614)
	ACWY-PS vaccine	216	87.5% (82.3; 91.6)	2633 (2299; 3014)	283	85.5% (80.9; 89.4)	2461 (2081; 2911)
Y	NIMENRIX	657	93.8% (91.6; 95.5)	14086 (13168; 15069)	862	87.0% (84.6; 89.2)	7711 (7100; 8374)
	ACWY-PS vaccine	219	78.5% (72.5; 83.8)	5066 (4463; 5751)	288	78.8% (73.6; 83.4)	4314 (3782; 4921)

The analysis of immunogenicity was conducted on the ATP cohorts

(1) Blood sampling performed 1 month post vaccination

VR: vaccine response, defined as the proportion of subjects with:

- rSBA titres ≥ 32 for initially seronegative subjects (i.e., pre-vaccination rSBA titre <8)
- or at least a 4-fold increase in rSBA titres from pre- to post-vaccination for initially seropositive subjects (i.e., pre vaccination rSBA titre ≥8)

*rSBA analysis performed at GSK laboratories

N = number of subjects with available results

GMT = geometric mean antibody titre

Persistence of immune response

In Study MenACWY-TT-048, the persistence of rSBA and hSBA titres was evaluated up to 4 years after vaccination in toddlers primed in study MenACWY-TT-039. Results are shown in Table 8.

Table 8: rSBA and hSBA titres up to 4 years following NIMENRIX (or MenC-CRM) in toddlers aged 12-23 months (Study MenACWY-TT-048)

Meningococcal Group	Vaccine group	Time-point (Years)	rSBA*			hSBA**		
			N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	3	262	59.9% (53.7; 65.9)	19.3 (15.7; 23.6)	251	35.9% (29.9; 42.1)	5.8 (4.8; 7.0)
		4	224	74.1% (67.9; 79.7)	107 (77.6; 148)	198	28.8% (22.6; 35.6)	4.9 (4.0; 6.0)
C	NIMENRIX	3	262	35.9% (30.1; 42.0)	9.8 (8.1; 11.7)	253	78.3% (72.7; 83.2)	37.8 (29.4; 48.6)
		4	225	40.4% (34.0; 47.2)	12.3 (9.8; 15.3)	209	73.2% (66.7; 79.1)	32.0 (23.8; 43.0)
	MenC-CRM vaccine	3	46	13.0% (4.9; 26.3)	5.7 (4.2; 7.7)	31	41.9% (24.5; 60.9)	6.2 (3.7; 10.3)
		4	45	35.6% (21.9; 51.2)	13.5 (7.4; 24.5)	32	46.9% (29.1; 65.3)	11.3 (4.9; 25.6)
W-135	NIMENRIX	3	261	49.8% (43.6; 56.0)	24.9 (19.2; 32.4)	254	82.3% (77.0; 86.8)	52.0 (41.4; 65.2)
		4	225	49.3% (42.6; 56.1)	30.5 (22.4; 41.5)	165	80.6% (73.7; 86.3)	47.1 (35.7; 62.2)
Y	NIMENRIX	3	262	53.8% (47.6; 60.0)	22.3 (17.6; 28.4)	250	72.0% (66.0; 77.5)	33.2 (25.9; 42.5)
		4	225	58.2% (51.5; 64.7)	36.2 (27.1; 48.4)	130	65.4% (56.5; 73.5)	29.8 (20.2; 44.1)

The analysis of immunogenicity was conducted on the ATP cohort for persistence adapted for each time-point.

*rSBA analysis performed at PHE laboratories in UK

**hSBA analysis performed at GSK laboratories

rSBA and hSBA titres were determined over a period of 10 years in children initially vaccinated with one dose of NIMENRIX or MenC-CRM at 12 to 23 months of age in Study MenACWY-TT-027. Persistence of SBA titres was evaluated in two extension studies: MenACWY-TT-032 (up to 5 years) and MenACWY-TT-100 (up to 10 years). Study MenACWY-TT-100 also evaluated the response to a single booster dose of NIMENRIX administered 10 years following the initial vaccination with NIMENRIX or MenC-CRM. Results are shown in Table 9 (see section 4.4 Special warnings and precautions for use).

Table 9: rSBA and hSBA titres following a single dose of NIMENRIX (or MenC-CRM) in toddlers aged 12-23 months, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-027/032/100)

Meningococcal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	Month 1[1]	222	100% (98.4; 100)	3707 (3327; 4129)	217	91.2% (86.7; 94.6)	59.0 (49.3; 70.6)
		Year 4[2]	45	64.4% (48.8; 78.1)	35.1 (19.4; 63.4)	44	52.3% (36.7; 67.5)	8.8 (5.4; 14.2)
		Year 5[2]	49	73.5% (58.9; 85.1)	37.4 (22.1; 63.2)	45	35.6% (21.9; 51.2)	5.2 (3.4; 7.8)
		Year 10[3] (Pre-booster)	62	66.1% (53.0; 77.7)	28.9 (16.4; 51.0)	59	25.4% (15.0; 38.4)	4.2 (3.0; 5.9)
		(Post-booster)[3,4]	62	98.4% (91.3; 100)	5122 (3726; 7043)	62	100% (94.2; 100)	1534 (1112; 2117)
C	NIMENRIX	Month 1[1]	220	100% (98.3; 100)	879 (779; 991)	221	99.1% (96.8; 99.9)	190 (165; 219)
		Year 4[2]	45	97.8% (88.2; 99.9)	110 (62.7; 192)	45	97.8% (88.2; 99.9)	370 (214; 640)
		Year 5[2]	49	77.6% (63.4; 88.2)	48.9 (28.5; 84.0)	48	91.7% (80.0; 97.7)	216 (124; 379)
		Year 10[3] (Pre-booster)	62	82.3% (70.5; 90.8)	128 (71.1; 231)	60	91.7% (81.6; 97.2)	349 (197; 619)
		(Post-booster)[3,4]	62	100% (94.2; 100)	7164 (5478; 9368)	59	100% (93.9; 100)	33960 (23890; 48274)
	MenC-CRM vaccine	Month 1[1]	68	98.5% (92.1; 100)	415 (297; 580)	68	72.1% (59.9; 82.3)	21.2 (13.9; 32.3)
		Year 4[2]	10	80.0% (44.4; 97.5)	137 (22.6; 832)	10	70.0% (34.8; 93.3)	91.9 (9.8; 859)
		Year 5[2]	11	63.6% (30.8; 89.1)	26.5 (6.5; 107)	11	90.9% (58.7; 99.8)	109 (21.2; 557)
		Year 10[3] (Pre-booster)	16	87.5% (61.7; 98.4)	86.7 (29.0; 259)	15	93.3% (68.1; 99.8)	117 (40.0; 344)
		(Post-booster)[3,4]	16	100% (79.4; 100)	5793 (3631; 9242)	15	100% (78.2; 100)	42559 (20106; 90086)
W-135	NIMENRIX	Month 1[1]	222	100% (98.4; 100)	5395 (4870; 5976)	177	79.7% (73.0; 85.3)	38.8 (29.7; 50.6)
		Year 4[2]	45	60.0% (44.3; 74.3)	50.8 (24.0; 108)	45	84.4% (70.5; 93.5)	76.9 (44.0; 134)
		Year 5[2]	49	34.7% (21.7; 49.6)	18.2 (9.3; 35.3)	46	82.6% (68.6; 92.2)	59.7 (35.1; 101)
		Year 10[3] (Pre-booster)	62	30.6% (19.6; 43.7)	15.8 (9.1; 27.6)	52	44.2% (30.5; 58.7)	7.7 (4.9; 12.2)
		(Post-booster)[3,4]	62	100% (94.2; 100)	25911 (19120; 35115)	62	100% (94.2; 100)	11925 (8716; 16316)
Y	NIMENRIX	Month 1[1]	222	100% (98.4; 100)	2824 (2529; 3153)	201	66.7% (59.7; 73.1)	24.4 (18.6; 32.1)
		Year 4[2]	45	62.2% (46.5; 76.2)	44.9 (22.6; 89.3)	41	87.8% (73.8; 95.9)	74.6 (44.5; 125)
		Year 5[2]	49	42.9% (28.8; 57.8)	20.6 (10.9; 39.2)	45	80.0% (65.4; 90.4)	70.6 (38.7; 129)

Meningococcal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	**≥8 (95%CI)**	**GMT (95%CI)**	**N**	**≥8 (95%CI)**	**GMT (95%CI)**
		Year 10[3] (Pre-booster)	62	45.2% (32.5; 58.3)	27.4 (14.7; 51.0)	56	42.9% (29.7; 56.8)	9.1 (5.5; 15.1)
		(Post-booster)[3,4]	62	98.4% (91.3; 100)	7661 (5263; 11150)	61	100% (94.1; 100)	12154 (9661; 15291)

(1) Study MenACWY-TT-027 (1 month post vaccination cohort)

(2) Study MenACWY-TT-032 (Year 4 and Year 5 data are for the Year 5 ATP cohort)

(3) Study MenACWY-TT-100 (booster ATP cohort)

(4) Blood sampling was performed 1 month after a booster dose at Year 10.

*rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for subsequent sampling time points.

**hSBA analysis performed at GSK laboratories and at Neomed in Canada for time points in Study MenACWY-TT 100.

Persistence of booster response

Study MenACWY-TT-102 evaluated the persistence of SBA titres up to 6 years after a booster dose of NIMENRIX or MenC-CRM$_{197}$ administered in Study MenACWY-TT-048 to children who initially received the same vaccine at 12 to 23 months of age in Study MenACWY-TT-039. A single booster dose was administered 4 years after the initial vaccination. Results are shown in Table 10 (see Section 4.4 Special warnings and precautions for use).

Table 10: rSBA and hSBA titres following a single dose of Nimenrix (or MenC-CRM) in toddlers aged 12-23 months, persistence at 4 years and response following a booster 4 years after initial vaccination, and persistence up to 6 years following booster vaccination (Studies MenACWY-TT-039/048/102)

Meningo-coccal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	NIMENRIX	Month 1[1]	354	99.7% (98.4; 100)	2205 (2008; 2422)	338	77.2% (72.4; 81.6)	19.0 (16.4; 22.1)
		Year 4[2] (Pre-Nimenrix booster)	212	74.5% (68.1; 80.2)	112 (80.3; 156)	187	28.9% (22.5; 35.9)	4.8 (3.9; 5.9)
		(Post-booster)[2,3]	214	100% (98.3; 100)	7173 (6389; 8054)	202	99.5% (97.3; 100)	1343 (1119; 1612)
		5 years after booster dose[4]	137	89.8% (83.4; 94.3)	229 (163; 322)	135	53.3% (44.6; 62.0)	13.2 (9.6; 18.3)
		6 years after booster dose[4]	134	92.5% (86.7; 96.4)	297 (214; 413)	130	58.5% (49.5; 67.0)	14.4 (10.5; 19.7)
C	NIMENRIX	Month 1[1]	354	99.7% (98.4; 100)	478 (437; 522)	341	98.5% (96.6; 99.5)	196 (175; 219)
		Year 4[2] (Pre-Nimenrix booster)	213	39.9% (33.3; 46.8)	12.1 (9.6; 15.2)	200	73.0% (66.3; 79.0)	31.2 (23.0; 42.2)
		(Post-booster)[2,3]	215	100% (98.3; 100)	4512 (3936; 5172)	209	100% (98.3; 100)	15831 (13626; 18394)
		5 years after booster dose[4]	137	80.3% (72.6; 86.6)	66.0 (48.1; 90.5)	136	99.3% (96.0; 100)	337 (261; 435)
		6 years after booster dose[4]	134	71.6% (63.2; 79.1)	39.6 (28.6; 54.6)	130	97.7% (93.4; 99.5)	259 (195; 345)
	MenC-CRM vaccine	Month 1[1]	121	97.5% (92.9; 99.5)	212 (170; 265)	116	81.9% (73.7; 88.4)	40.3 (29.5; 55.1)
		Year 4[2] (Pre-MenC-CRM_{197} booster)	43	37.2% (23.0; 53.3)	14.3 (7.7; 26.5)	31	48.4% (30.2; 66.9)	11.9 (5.1; 27.6)
		(Post-booster)[2,3]	43	100% (91.8; 100)	3718 (2596; 5326)	33	100% (89.4; 100)	8646 (5887; 12699)
		5 years after booster dose[4]	23	78.3% (56.3; 92.5)	47.3 (19.0; 118)	23	100% (85.2; 100)	241 (139; 420)
		6 years after booster dose[4]	23	65.2% (42.7; 83.6)	33.0 (14.7; 74.2)	23	95.7% (78.1; 99.9)	169 (94.1; 305)
W-135	NIMENRIX	Month 1[1]	354	100% (99.0; 100)	2682 (2453; 2932)	336	87.5% (83.5; 90.8)	48.9 (41.2; 58.0)
		Year 4[2] (Pre-Nimenrix booster)	213	48.8% (41.9; 55.7)	30.2 (21.9; 41.5)	158	81.6% (74.7; 87.3)	48.3 (36.5; 63.9)
		(Post-booster)[2,3]	215	100% (98.3; 100)	10950 (9531; 12579)	192	100% (98.1; 100)	14411 (12972; 16010)
		5 years after booster dose[4]	137	88.3% (81.7; 93.2)	184 (130; 261)	136	100% (97.3; 100)	327 (276; 388)
		6 years after booster dose[4]	134	85.8% (78.7; 91.2)	172 (118; 251)	133	98.5% (94.7; 99.8)	314 (255; 388)

Table 10: rSBA and hSBA titres following a single dose of Nimenrix (or MenC-CRM) in toddlers aged 12-23 months, persistence at 4 years and response following a booster 4 years after initial vaccination, and persistence up to 6 years following booster vaccination (Studies MenACWY-TT-039/048/102)

Meningo-coccal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
Y	NIMENRIX	Month 1[(1)]	354	100% (99.0; 100)	2729 (2473; 3013)	329	79.3% (74.5; 83.6)	30.9 (25.8; 37.1)
		Year 4[(2)] (Pre-Nimenrix booster)	213	58.2% (51.3; 64.9)	37.3 (27.6; 50.4)	123	65.9% (56.8; 74.2)	30.2 (20.2; 45.0)
		(Post-booster)[(2,3)]	215	100% (98.3; 100)	4585 (4129; 5093)	173	100% (97.9; 100)	6776 (5961; 7701)
		5 years after booster dose[(4)]	137	92.7% (87.0; 96.4)	265 (191; 368)	137	97.8% (93.7; 99.5)	399 (321; 495)
		6 years after booster dose[(4)]	134	94.0% (88.6; 97.4)	260 (189; 359)	131	97.7% (93.5; 99.5)	316 (253; 394)

The analysis of immunogenicity was conducted on the ATP cohort for each time point.

(1) Study MenACWY-TT-039

(2) Study MenACWY-TT-048

(3) Blood sampling was performed 1 month after a booster dose at Year 4.

(4) Study MenACWY-TT-102

*rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for the subsequent sampling time points.

**hSBA analysis performed at GSK laboratories and at Neomed in Canada for time points in Study MenACWY-TT-102.

Persistence of immune response in children aged 2-10 years

In Study MenACWY-TT-088, the persistence of SBA titres was evaluated up to 68 months after vaccination in children 2-10 years of age initially vaccinated in Study MenACWY-TT-081. Results are shown in Table 11 below.

Table 11: rSBA and hSBA titres up to 68 months persistence data following NIMENRIX (or MenC-CRM) in children aged 2-10 years of age at time of vaccination (Study MenACWY-TT-088)

Meningococcal Group	Vaccine group	Time-point (months)	rSBA*			hSBA**		
			N	≥8 (95%CI)	GMT (95%CI)	N***	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	32	193	86.5% (80.9; 91.0)	196 (144; 267)	90	25.6% (16.9; 35.8)	4.6 (3.3; 6.3)
		68	178	86.5% (80.6; 91.2)	129 (93.5; 179)	170	40.6% (33.1; 48.4)	6.9 (5.4; 8.9)
C	NIMENRIX	32	192	64.6% (57.4; 71.3)	34.8 (26.0; 46.4)	90	95.6% (89.0; 98.8)	75.9 (53.4; 108)
		68	178	39.9% (32.6; 47.5)	14.2 (10.8; 18.7)	172	75.6% (68.5; 81.8)	28.4 (21.2; 37.9)
	MenC-CRM vaccine	32	69	76.8% (65.1; 86.1)	86.5 (47.3; 158)	33	90.9% (75.7; 98.1)	82.2 (34.6; 196)
		68	61	62.3% (49.0; 74.4)	44.5 (23.7; 83.6)	57	75.4% (62.2; 85.9)	34.3 (19.0; 61.9)
W-135	NIMENRIX	32	193	77.2% (70.6; 82.9)	214 (149; 307)	86	84.9% (75.5; 91.7)	69.9 (48.2; 101)
		68	178	52.8%	59.2	159	78.6%	56.7

Meningococcal Group	Vaccine group	Time-point (months)	rSBA*			hSBA**		
			N	≥8 (95%CI)	GMT (95%CI)	N***	≥8 (95%CI)	GMT (95%CI)
				(45.2; 60.3)	(39.3; 89.2)		(71.4; 84.7)	(41.5; 77.3)
Y	NIMENRIX	32	193	81.3% (75.1; 86.6)	227 (165; 314)	91	81.3% (71.8; 88.7)	79.2 (52.5; 119)
		68	178	71.3% (64.1; 77.9)	139 (96.0; 202)	159	73.0% (65.3; 79.7)	56.3 (39.5; 80.3)

The analysis of immunogenicity was conducted on the ATP cohort for persistence adapted for each time point.

*rSBA analysis performed at PHE laboratories in UK

**hSBA analysis performed at GSK laboratories

*** at Month 32, a subset of subjects has been tested for hSBA

Persistence of immune response in children aged 6-10 years at vaccination

In Study MenACWY-TT-028, the persistence of hSBA titres was evaluated 1 year after vaccination in children aged 6-10 years of age who were initially vaccinated with either NIMENRIX or ACWY-PS vaccine in Study MenACWY-TT-027. Results are shown in Table 12.

Table 12: hSBA* titres following a single dose of NIMENRIX (or ACWY-PS) in children aged 6-10 and persistence 1 year following vaccination (Studies MenACWY-TT-027/028)

Meningococcal group	Vaccine group	1 month post vaccination (Study MenACWY-TT-027)			1 year persistence (Study MenACWY-TT-028)		
		N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	105	80.0 % (71.1; 87.2)	53.4 (37.3; 76.2)	104	16.3% (9.8; 24.9)	3.5 (2.7; 4.4)
	ACWY-PS vaccine	35	25.7% (12.5;43.3)	4.1 (2.6;6.5)	35	5.7% (0.7;19.2)	2.5 (1.9;3.3)
C	NIMENRIX	101	89.1% (81.3;94.4)	155.8 (99.3;244)	105	95.2% (89.2;98.4)	129.5 (95.4;176)
	ACWY-PS vaccine	38	39.5% (24.0;56.6)	13.1 (5.4;32.0)	31	32.3% (16.7;51.4)	7.7 (3.5;17.3)
W-135	NIMENRIX	103	95.1% (89.0;98.4)	133.5 (99.9;178)	103	100% (96.5;100)	256.7 (218.2;302)
	ACWY-PS vaccine	35	34.3% (19.1;52.2)	5.8 (3.3;9.9)	31	12.9% (3.6;29.8)	3.4 (2.0;5.8)
Y	NIMENRIX	89	83.1% (73.7;90.2)	95.1 (62.4;145.1)	106	99.1% (94.9;100)	265.0 (213;330)
	ACWY-PS vaccine	32	43.8% (26.4;62.3)	12.5 (5.6;27.7)	36	33.3% (18.6;51.0)	9.3 (4.3;19.9)

The analysis of immunogenicity was conducted on the ATP cohort for persistence at Year 1.

hSBA analysis was not performed for children aged 2 to <6 years (at time of vaccination).

*hSBA analysis performed at GSK Laboratories

SBA titres were determined over a period of 10 years in children initially vaccinated with one dose of NIMENRIX or ACWY-PS at 2 to 10 years of age in Study MenACWY-TT-027. Persistence of SBA titres was evaluated in two extension studies: MenACWY-TT-032 (up to 5 years) and MenACWY-TT-100 (up to 10 years). Study MenACWY-TT-100 also evaluated the response to a single booster dose of NIMENRIX administered 10 years

following the initial vaccination with NIMENRIX or ACWY-PS. Results are shown in Table 13 (see section 4.4 Special warnings and precautions for use).

Table 13: rSBA and hSBA titres following a single dose of NIMENRIX (or ACWY-PS) in children aged 2- 10 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-027/032/100)

Meningo-coccal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	NIMENRIX	Month 1[1]	225	100% (98.4; 100)	7301 (6586; 8093)	111[5]	81.1% (72.5; 87.9)	57.0 (40.3; 80.6)
		Year 5[2]	98	90.8% (83.3; 95.7)	141 (98.2; 203)	n/a[6]	--	--
		Year 6[3]	98	79.6% (70.3; 87.1)	107 (66.0; 174)	90	41.1% (30.8; 52.0)	6.5 (4.8; 8.8)
		Year 10[3] (Pre-booster)	73	89.0% (79.5; 95.1)	96.3 (57.1; 163)	62	33.9% (22.3; 47.0)	4.5 (3.3; 6.2)
		(Post-booster)[3,4]	74	95.9% (88.6; 99.2)	4626 (3041; 7039)	73	100% (95.1; 100)	1213 (994; 1481)
	ACWY-PS vaccine	Month 1[1]	75	100% (95.2; 100)	2033 (1667; 2480)	35[5]	25.7% (12.5; 43.3)	4.1 (2.6; 6.5)
		Year 5[2]	13	15.4% (1.9; 45.4)	4.7 (3.7; 6.0)	n/a[6]	--	--
		Year 6[3]	24	12.5% (2.7; 32.4)	5.8 (3.5; 9.6)	21	33.3% (14.6; 57.0)	5.9 (3.0; 11.7)
		Year 10[3] (Pre-booster)	17	23.5% (6.8; 49.9)	8.0 (3.3; 19.3)	17	29.4% (10.3; 56.0)	6.2 (2.4; 15.7)
		(Post-booster)[3,4]	17	100% (80.5; 100)	6414 (3879; 10608)	17	100% (80.5; 100)	211 (131; 340)
C	NIMENRIX	Month 1[1]	225	100% (98.4; 100)	2435 (2106; 2816)	107[5]	89.7% (82.3; 94.8)	155 (101; 237)
		Year 5[2]	98	90.8% (83.3; 95.7)	79.7 (56.0; 113)	n/a[6]	--	--
		Year 6[3]	98	82.7% (73.7; 89.6)	193 (121; 308)	97	93.8% (87.0; 97.7)	427 (261; 700)
		Year 10[3] (Pre-booster)	74	85.1% (75.0; 92.3)	181 (106; 310)	73	91.8% (83.0; 96.9)	222 (129; 380)
		(Post-booster)[3,4]	74	100% (95.1; 100)	4020 (3319; 4869)	71	100% (94.9; 100)	15544 (11735; 20588)
	ACWY-PS vaccine	Month 1[1]	74	100% (95.1; 100)	750 (555; 1014)	38[5]	39.5% (24.0; 56.6)	13.1 (5.4; 32.0)
		Year 5[2]	13	100% (75.3; 100)	128 (56.4; 291)	n/a[6]	--	--
		Year 6[3]	24	79.2% (57.8; 92.9)	98.7 (42.2; 231)	24	100% (85.8; 100)	235 (122; 451)
		Year 10[3] (Pre-booster)	17	76.5% (50.1; 93.2)	96.2 (28.9; 320)	17	100% (80.5; 100)	99.1 (35.8; 274)
		(Post-booster)[3,4]	17	100% (80.5; 100)	15101 (7099; 32122)	17	94.1 (71.3; 99.9)	44794 (10112; 198440)
W-135	NIMENRIX	Month 1[1]	225	100% (98.4; 100)	11777 (10666; 13004)	107[5]	95.3% (89.4; 98.5)	134 (101; 178)
		Year 5[2]	98	78.6% (69.1; 86.2)	209 (128; 340)	n/a[6]	--	--
		Year 6[3]	98	73.5% (63.6; 81.9)	265 (155; 454)	92	81.5% (72.1; 88.9)	62.5 (42.0; 93.1)

Table 13: rSBA and hSBA titres following a single dose of NIMENRIX (or ACWY-PS) in children aged 2- 10 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-027/032/100)

		Year 10[3] (Pre-booster)	74	68.9% (57.1; 79.2)	206 (109; 392)	59	61.0% (47.4; 73.5)	17.5 (10.5; 29.2)
		(Post-booster)[3,4]	74	100% (95.1; 100)	27944 (22214; 35153)	74	100% (95.1; 100)	6965 (5274; 9198)
	ACWY-PS vaccine	Month 1[1]	75	100% (95.2; 100)	2186 (1723; 2774)	35[5]	34.3% (19.1; 52.2)	5.8 (3.3, 9.9)
		Year 5[2]	13	0% (0.0; 24.7)	4.0 (4.0; 4.0)	n/a[6]	--	--
		Year 6[3]	24	12.5% (2.7; 32.4)	7.6 (3.7; 15.6)	23	30.4% (13.2; 52.9)	7.0 (2.9; 16.9)
		Year 10[3] (Pre-booster)	17	23.5% (6.8; 49.9)	15.4 (4.2; 56.4)	15	26.7% (7.8; 55.1)	4.1 (2.0; 8.5)
		(Post-booster)[3,4]	17	94.1% (71.3; 99.9)	10463 (3254; 33646)	15	100% (78.2; 100)	200 (101; 395)
Y	**NIMENRIX**	Month 1[1]	225	100% (98.4; 100)	6641 (6044; 7297)	94[5]	83.0% (73.8; 89.9)	93.7 (62.1; 141)
		Year 5[2]	98	78.6% (69.1; 86.2)	143 (88.0; 233)	n/a[6]	--	--
		Year 6[3]	98	71.4% (61.4; 80.1)	136 (82.6; 225)	89	65.2% (54.3; 75.0)	40.3 (23.9; 68.1)
		Year 10[3] (Pre-booster)	74	67.6% (55.7; 78.0)	98.5 (54.3; 179)	65	72.3% (59.8; 82.7)	35.7 (21.0; 60.6)
		(Post-booster)[3,4]	74	100% (95.1; 100)	7530 (5828; 9729)	74	100% (95.1; 100)	11127 (8909; 13898)
	ACWY-PS vaccine	Month 1[1]	75	100% (95.2; 100)	1410 (1086; 1831)	32[5]	43.8% (26.4; 62.3)	12.5 (5.6; 27.7)
		Year 5[2]	13	7.7% (0.2; 36.0)	5.5 (2.7; 11.1)	n/a[6]	--	--
		Year 6[3]	24	20.8% (7.1; 42.2)	11.6 (4.7; 28.7)	24	25.0% (9.8; 46.7)	7.3 (2.7; 19.8)
		Year 10[3] (Pre-booster)	17	17.6% (3.8; 43.4)	10.2 (3.5; 30.2)	14	35.7% (12.8; 64.9)	7.8 (2.5; 24.4)
		(Post-booster)[3,4]	17	100% (80.5; 100)	6959 (3637; 13317)	17	100% (80.5; 100)	454 (215; 960)

The analysis of immunogenicity was conducted on the ATP cohort for each time point.

(1) Study MenACWY-TT-027
(2) Study MenACWY-TT-032
(3) Study MenACWY-TT-100
(4) Blood sampling was performed 1 month after a booster dose at Year 10.
(5) Includes children aged 6 to <11 years. hSBA analysis was not performed for children aged 2 to <6 years (at time of vaccination).
(6) Per the protocol for Study MenACWY-TT-032, hSBA was not measured for this age group at Year 5.

*rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for subsequent sampling time points.

**hSBA analysis performed at GSK laboratories and at Neomed in Canada for time points in Study MenACWY-TT-100.

Persistence of immune response in adolescents aged 11-17 years at vaccination

rSBA titres were determined over a period of 10 years in subjects initially vaccinated with one dose of NIMENRIX or ACWY-PS at 11 to 17 years of age in Study MenACWY-TT-036. Persistence of rSBA titres was evaluated in two extension studies: MenACWY-TT-043 (up to 5 years) and MenACWY-TT-101 (at 10 years). Study MenACWY-TT-101 also evaluated the response to a single booster dose of NIMENRIX administered 10 years following the initial vaccination with NIMENRIX or ACWY-PS. Results are shown in Table 14.

Table 14: rSBA* titres following a single dose of NIMENRIX (or ACWY-PS) in adolescents aged 11-17 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-036/043/101)

Meningococcal group	Time-point	NIMENRIX			ACWY-PS vaccine		
		N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	Month 1[1]	674	100% (99.5; 100)	5929 (5557; 6324)	224	99.6% (97.5; 100)	2947 (2612; 3326)
	Year 3[2]	449	92.9% (90.1; 95.1)	448 (381; 527)	150	82.7% (75.6; 88.4)	206 (147; 288)
	Year 5[2]	236	97.5 % (94.5; 99.1)	644 (531; 781)	86	93.0 (85.4; 97.4)	296 (202; 433)
	Year 10[3] (Pre-booster)	162	85.2% (78.8; 90.3)	248 (181; 340)	51	80.4% (66.9; 90.2)	143 (80.5; 253)
	(Post-booster)[3,4]	162	100% (97.7; 100)	3760 (3268; 4326)	51	100% (93.0; 100)	2956 (2041; 4282)
C	Month 1[1]	673	100% (99.5; 100)	13110 (11939; 14395)	224	100% (98.4; 100)	8222 (6808; 9930)
	Year 3[2]	449	91.1% (88.1; 93.6)	371 (309; 446)	150	86.0% (79.4; 91.1)	390 (262; 580)
	Year 5[2]	236	88.6 % (83.8; 92.3)	249 (194; 318)	85	87.1 (78.0; 93.4)	366 (224; 599)
	Year 10[3] (Pre-booster)	162	90.1% (84.5; 94.2)	244 (182; 329)	51	82.4% (69.1; 91.6)	177 (86.1; 365)
	(Post-booster)[3,4]	162	100% (97.7; 100)	8698 (7391 10235)	51	100% (93.0; 100)	3879 (2715; 5544)
W-135	Month 1[1]	678	99.9% (99.2; 100)	8247 (7639; 8903)	224	100% (98.4; 100)	2633 (2299; 3014)
	Year 3[2]	449	82.0% (78.1; 85.4)	338 (268; 426)	150	30.0% (22.8; 38.0)	16.0 (10.9; 23.6)
	Year 5[2]	236	86.0% (80.9; 90.2)	437 (324; 588)	86	34.9 (24.9; 45.9)	19.7 (11.8; 32.9)
	Year 10[3] (Pre-booster)	162	71.6% (64.0; 78.4)	146 (97.6; 217)	51	43.1% (29.3; 57.8)	16.4 (9.2; 29.4)
	(Post-booster)[3,4]	162	100% (97.7; 100)	11243 (9367; 13496)	51	100% (93.0; 100)	3674 (2354; 5734)
Y	Month 1[1]	677	100% (99.5; 100)	14087 (13168; 15069)	224	100% (98.4; 100)	5066 (4463; 5751)
	Year 3[2]	449	93.1% (90.3; 95.3)	740 (620; 884)	150	58.0% (49.7; 66.0)	69.6 (44.6; 109)
	Year 5[2]	236	96.6% (93.4; 98.5)	1000 (824; 1214)	86	66.3 (55.3; 76.1)	125 (71.2; 219)

Meningococcal group	Time-point	NIMENRIX			ACWY-PS vaccine		
		N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
	Year 10[3] (Pre-booster)	162	90.7% (85.2; 94.7)	447 (333; 599)	51	49.0% (34.8; 63.4)	32.9 (17.1; 63.3)
	(Post-booster)[3,4]	162	100% (97.7; 100)	7585 (6748; 8525)	51	98.0% (89.6; 100)	3296 (1999; 5434)

The analysis of immunogenicity was conducted on the ATP cohort for each time point.

(1) Study MenACWY-TT-036
(2) Study MenACWY-TT-043
(3) Study MenACWY-TT-101
(4) Blood sampling was performed 1 month after a booster dose at Year 10.

*rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for the subsequent sampling time points.

Persistence of immune response in adolescents and adults aged 11-25 years at vaccination

In Study MenACWY-TT-059, hSBA persistence was evaluated up to 5 years after vaccination in adolescents and adults aged 11-25 years initially vaccinated in Study MenACWY-TT-052.

For all meningococcal groups, the persistence of hSBA titres elicited by NIMENRIX was similar to or higher than those induced by the licensed quadrivalent meningococcal diphtheria toxoid (DT) conjugate vaccine (ACWY-DT) as shown in Table 15.

Table 15: hSBA* titres following a single dose of NIMENRIX (or ACWY-DT) 1 month post-vaccination and 5 years persistence data (hSBA*) in adolescents and adults aged 11-25 years of age

Meningococcal Group	Vaccine group	Timepoint	N	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	Month 1[1]	356	82.0% (77.6; 85.9)	58.7 (48.6; 70.9)
		Year 1[2]	350	29.1% (24.4; 34.2)	5.4 (4.5; 6.4)
		Year 5[2]	141	48.9 % (40.4; 57.5)	8.9 (6.8; 11.8)
	ACWY-DT	Month 1[1]	107	73.8% (64.4; 81.9)	42.5 (28.5; 63.3)
		Year 1[2]	111	31.5% (23.0; 41.0)	6.0 (4.3; 8.5)
		Year 5[2]	45	44.4% (29.6; 60.0)	7.9 (4.8; 13.2)
C	NIMENRIX	Month 1[1]	359	96.1% (93.5; 97.9)	532 (424; 668)
		Year 1[2]	336	94.9% (92.0; 97.0)	172 (142; 207)
		Year 5[2]	140	92.9% (87.3; 96.5)	94.6 (65.9; 136)
	ACWY-DT	Month 1[1]	113	99.1% (95.2; 100)	317 (217; 462)
		Year 1[2]	105	73.3% (63.8; 81.5)	46.7 (30.2; 72.1)
		Year 5[2]	44	79.5% (64.7; 90.2)	30.6 (17.3; 54.4)
W-135	NIMENRIX	Month 1[1]	334	91.0% (87.4; 93.9)	117 (96.8; 141)
		Year 1[2]	327	98.5% (96.5; 99.5)	197 (173; 225)
		Year 5[2]	138	87.0% (80.2; 92.1)	103 (76.3; 140)
	ACWY-DT	Month 1[1]	96	75.0% (65.1; 83.3)	70.4 (43.7; 113)
		Year 1[2]	107	75.7% (66.5; 83.5)	48.9 (32.5; 73.8)
		Year 5[2]	44	84.1% (69.9; 93.4)	70.4 (37.2; 133)
Y	NIMENRIX	Month 1[1]	364	95.1% (92.3; 97.0)	246 (208; 291)

Meningococcal Group	Vaccine group	Timepoint	N	≥8 (95%CI)	GMT (95%CI)
		Year 1[(2)]	356	97.8% (95.6; 99.0)	272 (237; 311)
		Year 5[(2)]	142	94.4% (89.2; 97.5)	225 (174; 290)
	ACWY-DT	Month 1[(1)]	111	81.1% (72.5; 87.9)	103 (67.5; 159)
		Year 1[(2)]	112	86.6% (78.9; 92.3)	101 (69.6; 146)
		Year 5[(2)]	44	90.9% (78.3; 97.5)	129 (77.4; 216)

The analysis of immunogenicity was conducted on the ATP cohort for persistence adapted for each time point.

(1) Study MenACWY-TT-052

(2) Study MenACWY-TT-059

*hSBA analysis performed at GSK laboratories

rSBA titres were determined over a period of 10 years in subjects initially vaccinated with one dose of NIMENRIX or ACWY-PS at 11 to 55 years of age in Study MenACWY-TT-015. Persistence of rSBA titres was evaluated in two extension studies: MenACWY-TT-020 (up to 5 years) and MenACWY-TT-099 (up to 10 years). Study MenACWY-TT-099 also evaluated the response to a single booster dose of NIMENRIX administered 10 years following the initial vaccination with NIMENRIX or ACWY-PS. Results are shown in Table 16.

Table 16: rSBA* titres following a single dose of NIMENRIX or ACWY-PS) in adolescents and adults aged 11-55 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-015/020/099)

Meningo-coccal group	Time point	NIMENRIX			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Month 1[(1)]	323	100% (98.9; 100)	4945 (4452, 5493)	112	100% (96.8, 100)	2190 (1858, 2582)
	Year 4[(2)]	43	95.3% (84.2; 99.4)	365 (226; 590)	17	76.5% (50.1; 93.2)	104 (31.0; 351)
	Year 5[(2)]	51	84.3% (71.4; 93.0)	190 (108; 335)	19	57.9% (33.5; 79.7)	37.0 (12.6; 109)
	Year 10[(3)] (Pre-booster)	155	78.1% (70.7; 84.3)	154 (108; 219)	52	71.2% (56.9; 82.9)	75.1 (41.4; 136)
	(Post-booster)[(3,4)]	155	100% (97.6; 100)	4060 (3384; 4870)	52	100% (93.2; 100)	3585 (2751; 4672)
C	Month 1[(1)]	341	99.7% (98.4; 100)	10074 (8700, 11665)	114	100% (96.8; 100)	6546 (5048; 8488)
	Year 4[(2)]	43	76.7% (61.4; 88.2)	126 (61.6; 258)	17	41.2% (18.4; 67.1)	16.7 (5.7; 48.7)
	Year 5[(2)]	51	72.5% (58.3; 84.1)	78.5 (41.8; 147)	18	38.9% (17.3; 64.3)	17.3 (6.0; 49.7)
	Year 10[(3)] (Pre-booster)	154	90.9% (85.2; 94.9)	193 (141; 264)	52	88.5% (76.6; 95.6)	212 (110; 412)
	(Post-booster)[(3,4)]	155	100% (97.6; 100)	13824 (10840; 17629)	52	98.1% (89.7; 100)	3444 (1999; 5936)
W-135	Month 1[(1)]	340	99.7% (98.4; 100)	8577 (7615; 9660)	114	100% (96.8; 100)	2970 (2439; 3615)
	Year 4[(2)]	43	90.7% (77.9; 97.4)	240 (128; 450)	17	17.6% (3.8; 43.4)	8.3 (3.6; 19.5)

Meningo-coccal group	Time point	NIMENRIX			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
	Year 5[2]	51	86.3% (73.7; 94.3)	282 (146; 543)	19	31.6% (12.6; 56.6)	15.4 (5.7; 41.9)
	Year 10[3] (Pre-booster)	154	71.4% (63.6; 78.4)	166 (107; 258)	52	21.2% (11.1; 34.7)	10.9 (6.1; 19.3)
	(Post-booster)[3,4]	155	100% (97.6; 100)	23431 (17351; 31641)	52	98.1% (89.7; 100)	5793 (3586; 9357)
Y	Month 1[1]	340	100% (98.9; 100)	10315 (9317; 11420)	114	100% (96.8; 100)	4574 (3864; 5414)
	Year 4[2]	43	86.0% (72.1; 94.7)	443 (230; 853)	17	47.1% (23.0; 72.2)	30.7 (9.0; 105)
	Year 5[2]	51	92.2% (81.1; 97.8)	770 (439; 1351)	19	63.2% (38.4; 83.7)	74.1 (21.9; 250)
	Year 10[3] (Pre-booster)	154	86.4% (79.9; 91.4)	364 (255; 519)	52	61.5% (47.0; 74.7)	56.0 (28.8; 109)
	(Post-booster)[3,4]	155	100% (97.6; 100)	8958 (7602; 10558)	52	100% (93.2; 100)	5138 (3528; 7482)

(1) Study MenACWY-TT-015 (1 month post vaccination ATP cohort)
(2) Study MenACWY-TT-020
(3) Study MenACWY-TT-099 (booster ATP cohort)
(4) Blood sampling was performed 1 month after a booster dose at Year 10.

*rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for the subsequent sampling time points.

In a descriptive study conducted in 194 adults aged 56 years and older (Study MenACWY-TT-085), NIMENRIX was immunogenic, with a vaccine response rate ≥ 63.4% and with ≥ 97.4% of subjects with rSBA titres ≥ 8 against all four meningococcal groups. Moreover, at least 93.2% of subjects achieved the more conservative threshold of protection of rSBA titres ≥ 128.

Immune memory

In Study MenACWY-TT-014, the induction of immune memory was assessed 1 month after the administration of a fifth of the dose of ACWY-PS vaccine (10 µg of each polysaccharide) to children in the third year of life. These children were initially vaccinated in study MenACWY-TT-013 with either NIMENRIX or a licensed MenC-CRM vaccine at the age of 12 to 14 months.

One month after the challenge dose, the GMTs elicited by the initial vaccination with NIMENRIX increased 6.5 to 8-fold, indicating that NIMENRIX induces immune memory to all four groups A, C, W-135 and Y. The post-challenge rSBA-MenC GMT was similar in both study groups, indicating that NIMENRIX induces an analogous immune memory to group C as the licensed MenC-CRM vaccine. Results are shown in Table 17.

Table 17: rSBA* titres 1 month after a challenge vaccination in subjects initially vaccinated with NIMENRIX or a MenC-CRM vaccine at the age of 12 to 14 months (Study MenACWY-TT-014)

Meningococcal group	Vaccine group	Pre-challenge		Post-challenge	
		N	GMT (95%CI)	N	GMT (95%CI)
A	NIMENRIX	32	544 (325; 911)	25	3322 (2294; 4810)
C	NIMENRIX	31	174 (105; 289)	32	5966 (4128; 8621)
	MenC-CRM	28	34.4 (15.8; 75.3)	30	5265 (3437; 8065.1)
W-135	NIMENRIX	32	644 (394; 1052)	32	11058 (8587; 14240)
Y	NIMENRIX	32	440 (274; 706)	32	5737 (4216; 7806)

The analysis of immunogenicity was conducted on the ATP cohort
*rSBA analysis performed at GSK laboratories

Booster response for subjects previously vaccinated with a conjugate meningococcal vaccine against Neisseria meningitidis

NIMENRIX booster vaccination in subjects previously primed with a monovalent conjugate (MenC-CRM) or a quadrivalent polysaccharide (ACWY-PS) or a quadrivalent conjugate meningococcal vaccine (MenACWY-TT) was studied in subjects from 12 months of age onwards who received a booster vaccination. Robust anamnestic responses to the antigen(s) in the priming vaccine were observed (see Tables 10, 11, 14, 15, and 16).

Response to NIMENRIX in subjects previously vaccinated with a plain polysaccharide meningococcal vaccine against Neisseria meningitidis

In Study MenACWY-TT-021 conducted in subjects aged 4.5-34 years, the immunogenicity of NIMENRIX administered between 30 and 42 months after vaccination with a ACWY-PS vaccine was compared to the immunogenicity of NIMENRIX administered to age-matched subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years. The rSBA GMTs were significantly lower in the subjects who had received a dose of ACWY-PS vaccine 30-42 months prior to NIMENRIX. The clinical relevance of this observation is unknown since all subjects achieved rSBA titres ≥ 8 for all four meningococcal groups regardless of meningococcal vaccination history. Results are shown in Table 18.

Table 18: rSBA* titres 1 month after NIMENRIX vaccination in subjects according to their meningococcal vaccine history (Study MenACWY-TT-021)

Meningococcal group	Subjects vaccinated 30 to 42 months previously with ACWY-PS			Subjects who had not received a meningococcal vaccine in the preceding 10 years		
	N	rSBA ≥8 (95%CI)	GMT (95%CI)	N	rSBA ≥8 (95%CI)	GMT (95%CI)
A	146	100% (97.5; 100)	6868.8 (6045; 7805)	69	100% (94.8; 100)	13015 (10722; 15798)

Meningococcal group	Subjects vaccinated 30 to 42 months previously with ACWY-PS			Subjects who had not received a meningococcal vaccine in the preceding 10 years		
	N	rSBA ≥8 (95%CI)	GMT (95%CI)	N	rSBA ≥8 (95%CI)	GMT (95%CI)
C	169	100% (97.8; 100)	1946 (1583.3; 2391.1)	75	100% (95.2; 100)	5495 (4266; 7076)
W-135	169	100% (97.8; 100)	4636 (3942; 5451)	75	100% (95.2; 100)	9078 (7088; 11627)
Y	169	100% (97.8; 100)	77800 (6683; 9104)	75	100% (95.2; 100)	13895 (11186; 17261)

The analysis of immunogenicity was conducted on the ATP cohort

*rSBA analysis performed at GSK laboratories

Response to NIMENRIX in subjects at increased risk for meningococcal infections

Study MenACWY-TT-084 evaluated the immunogenicity of one and two doses of NIMENRIX given 2 months apart in 43 at-risk subjects aged 2-17 years (at increased risk for meningococcal disease, i.e., asplenic subjects, and hyposplenic subjects) compared to 43 healthy age-matched subjects.

One month after the first vaccine dose, vaccine response rates (rSBA titre ≥1:32 or a ≥4-fold increase in rSBA titre from baseline) for groups A, C, W-135, and Y, respectively, were 100%, 92.5%, 100% and 97.5% in the at-risk group and were 97.5%, 97.5%, 97.5%, and 100% for healthy subjects. After the second vaccine dose, vaccine response rates in both at-risk and healthy subjects were 100% for each of the four meningococcal groups.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on local tolerance, acute toxicity, repeated dose toxicity, developmental/reproductive toxicity and fertility studies.

Genotoxicity

No data available.

Carcinogenicity

The carcinogenic potential of NIMENRIX has not been investigated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:
Sucrose
Trometamol

Solvent:
0.9% Sodium chloride
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

After reconstitution:

After reconstitution, the vaccine should be used immediately. For shelf-life after reconstitution of the medicinal product, see Section 4.2 Use and handling.

6.4 Special precautions for storage

NIMENRIX must be stored between +2°C to +8°C. The sterile 0.9% saline diluent may be refrigerated or stored at ambient temperatures, but must not be frozen. The vaccine should be stored in the original package in order to protect from light.

6.5 Nature and contents of container

NIMENRIX is supplied in a single dose as a white lyophilised powder in a glass vial (type 1 glass) with a stopper (butyl rubber), together with 0.5mL solvent in a pre-filled syringe with a stopper (butyl rubber).

Pack sizes of 1 and 10 without separate needles.

Not all pack sizes or presentations may be marketed.

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical properties

Chemical structure

No data available.

CAS number

No data available.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

Pfizer Australia Pty Ltd
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Sydney NSW 2000
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9 DATE OF FIRST APPROVAL

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10 DATE OF REVISION

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Summary Table of Changes

Section changed	Summary of new information
4.8	Addition of ‘urticaria’ to Table 1: Adverse Reactions
8	Update to Sponsor email address